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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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09/175,683

10/20/1998

LI HOW CHEN

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11/21/2008

GTC BIOTHERAPEUTICS, INC.

C/O WOLF, GREENFIELD & SACKS, P.C.

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BOSTON, MA 02210-2206

EXAMINER

SCHNIZER, RICHARD A

ART UNIT

PAPER NUMBER

1635

MAIL DATE

DELIVERY MODE

11/21/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 09/175,683	Applicant(s) CHEN ET AL.	
	Examiner Richard Schnizer	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12 September 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 85-92 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 85-92 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>9/12/08</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after allowance or after an Office action under *Ex Parte Quayle*, 25 USPQ 74, 453 O.G. 213 (Comm'r Pat. 1935). Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 9/12/08 has been entered.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

The instant inventors have pending applications and issued patents with subject matter similar to that in the instant claims, i.e. applications 10/949,975 and 10/082,018, and US Patents 6,593,463 and 7,354,594.

Claims 85-92 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-27 of U.S. Patent No. 7,354,594. Although the conflicting claims are not identical, they are not patentably distinct from each other.

The '594 claims are drawn to compositions comprising a merozoite surface protein 1 or fragment thereof wherein at least one glycosylation site has been eliminated. Claims 6-27 explicitly require that the protein must be made in the milk of a non-human transgenic animal whose genome comprises a modified gene encoding the MSP-1 or fragment thereof operably linked to a mammary gland promoter, wherein the modification reduces the AT content of the gene by replacement of protozoan codons with codons preferred by mammalian cells. So, the proteins of the '594 patent could be made by the instantly claimed methods, and '594 claims 6-27 require that the proteins must be made methods embraced by the instant claims. Note that SEQ ID NO: 2, recited in '594 claims 6-27, encodes instant SEQ ID NO: 10, so the instant claims clearly embrace methods of making the protein of '594. Thus the invention as a whole was prima facie obvious.

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Claims 85-92 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 27-32, 34-37, 39-58, 60-67, 69-72, and 74 of copending Application No. 10/949,975.

The claims of '975 are drawn to:

methods for producing a parasite protein or fragment thereof in milk of a non-human transgenic mammal, comprising:

providing said non-human transgenic mammal whose genome comprises a modified nucleic acid sequence encoding said parasite protein or fragment thereof operably linked to a promoter which directs expression in a mammary gland,

wherein said modified nucleic acid sequence has been modified by replacing one or more AT-containing codons of the nucleic acid sequence of said parasite protein or fragment thereof as it naturally occurs in a parasite with a codon or codons preferred by a mammalian cell for the purposes of expression and encoding the same parasite protein or fragment thereof as derived from said parasite, and

wherein said modified nucleic acid sequence has been further modified such that at least one glycosylation site of the encoded parasite protein or fragment thereof has been eliminated; and

allowing said non-human transgenic mammal to express said parasite protein or fragment thereof in its milk, to thereby produce said parasite protein or fragment thereof (claims 27-37);

methods for producing a parasite protein or fragment thereof in the milk of a non-human transgenic mammal, comprising:

providing said non-human transgenic mammal whose genome comprises a modified nucleic acid sequence encoding said parasite protein or fragment thereof operably linked to a promoter which directs expression in a mammary gland,

wherein said nucleic acid sequence of said parasite protein or fragment thereof has been modified by replacing at least a portion of an AUUUA mRNA instability motif in a coding sequence of said parasite protein or fragment thereof as it naturally occurs in a parasite with a codon or codons preferred by a mammalian cell for the purposes of expression so as to remove said AUUUA mRNA instability motif or prevent said AUUUA mRNA instability motif from destabilizing mRNAs encoding said parasite protein or fragment thereof while encoding an amino acid which is the same as the replaced portion of said AUUUA mRNA instability motif, and

wherein said modified nucleic acid sequence has been further modified such that at least one glycosylation site of the encoded parasite protein or fragment thereof has been eliminated; and

allowing said non-human transgenic mammal to express said parasite protein or fragment thereof in its milk, to thereby produce said parasite protein or fragment thereof, and wherein the naturally occurring nucleic acid sequence encoding said parasite protein or fragment thereof contains at least one AUUUA instability motif (claims 39-45);

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methods combining the methods of claims 27-45 (claims 46-58); and to mammals made by the methods (claims 60-67, 69-72, and 74).

Accordingly the claims are species of the instant claims, and the instant claims are obvious in view of them.

The 10/082,018 application was allowed on 9/17/07, 12/10/07, and 6/5/08. The '018 application and the instant application have the same effective filing date. The allowed claims overlap the instant claims in scope, and a terminal disclaimer over the instant claims was filed in the '018 application. The instant claims are broader, so the instant application is considered to claim the "base invention" according to MPEP 804(I)(B)(1), so no terminal disclaimer over the '018 claims is required in the instant application. Note that a terminal disclaimer over US 7,354,594, will result in the instant application, the '018 application, and the '594 patent all being linked by terminal disclaimers.

US 6,593,463 claims nucleic acids useful for making transgenic animals. Claims to nucleic acids were restricted from claims to transgenic animals in the '463 prosecution history. The nucleic acids of '463 could be used to make the transgenic animals recited in the instant claims. However, these nucleic acids could be used for a another patentably distinct purpose such as producing the encoded protein in isolated cultured cells. Neither the instantly recited method steps nor the transgenic animals are considered obvious over a nucleic acid that could be used as a starting material, but which also has other uses, in the absence of secondary references and a motivation to combine them. It is noted that the instant specification and the specification of '463

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show that a native unmodified MSP-1 open reading frame was not expressed in mammalian cells, whereas the modified nucleic acids of the '463 claims allowed expression in a mammalian host. This is considered a secondary consideration sufficient to overcome an obviousness rejection based on combined references.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 571-272-0762. The examiner can normally be reached Monday through Friday between the hours of 6:00 AM and 3:30. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, James (Doug) Schultz, can be reached at (571) 272-0763. The official central fax number is 571-273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

/Richard Schnizer, Ph. D./
Primary Examiner, Art Unit 1635